

E! wherein the container has pores which permit diffusion of the protein between the interior and the exterior of the container. --

### REMARKS

Claims 69-112 are pending following entry of this Supplementary Preliminary Amendment. Claims 37, 38, and 55-68 have been canceled. Claims 69-112 have been added. These amendments do not include new matter, as set forth in the following section.

#### Support in the Specification

The changes made to the specification represent mere grammatical and spelling corrections that would be apparent to the skilled artisan. None of these changes is believed by the Applicants to be substantive.

Claims 69-108 recite containers which contain isolated bone marrow stromal cells, as disclosed throughout the specification, for example at page 1, lines 3-5. The specification discloses that the stromal cells comprise an expressible gene construct encoding a protein (e.g., at page 14, lines 8-10, and at page 7, lines 14-18) and that the container physically isolates the stromal cells from immune cells of an animal into which the container is implanted (e.g., at page 4, lines 20-22, and at page 6, line 24, through page 7, line 3). Containers having pores are disclosed, for example at page 6, line 36, through page 7, line 1, and at page 27, lines 1-5. Recitation in claim 69 that the pores are "for permitting diffusion between the interior and the exterior of the container" merely refers to the inherent function of the pores (disclosed, for example, at page 27, lines 4 and 5). Recitations of pore properties and sizes (e.g., in claims 71, 99-101, and 112) are disclosed in the specification (e.g., at page 27, lines 4 and 5, at page 27, lines 10-12, and at page 45, lines 21-24). Particular numbers of stromal cells (e.g., as recited in claims 107 and 108) are disclosed in the specification, for example at page 27, lines 16 and 17.

Use of gene constructs encoding secreted proteins (i.e., as recited in claim 70) is disclosed in the specification, for example at page 13, lines 17 and 18, and at page 15, lines 1-3. Particular proteins and types of proteins encoded by the recited

gene construct (e.g., as recited in claims 76-96) are disclosed throughout the specification, for example at page 16, lines 21-30, and in Tables IV and V (on pages 49 and 50, respectively). Use of the recited stromal cells for implantation into humans afflicted with various disease, disorders, and conditions (e.g., as recited in claims 74, 75, and 109-111) is disclosed in the specification, for example at page 15, lines 4-32. Use of stromal cells with expressible gene constructs encoding two different proteins (e.g., as recited in claims 102-104) is disclosed in the specification, for example at page 21, lines 30-37.

For the foregoing reasons, the Applicants contend that newly added claims 69-112 do not include new matter.

Response to the Office Action Dated June 20, 2000

The Applicants believe that the claim rejections made in the Office Action dated June 20, 2000 (Paper No. 19) are moot in view of the fact that the Applicants have canceled all of the claims that were pending at the time that Office Action was issued. Nonetheless, in an effort to expedite allowance of the pending claims, the Applicants explain in the following sections why those rejections are not applicable to newly added claims 69-110.

Rejection of Claim 58 Pursuant to 35 U.S.C. § 112

Claim 58 was rejected pursuant to 35 U.S.C. § 112, second paragraph. In the Examiner's view, the phrase "matched donor stromal cells" is indefinite. This term is not used in any of the newly added claims. This rejection is therefore moot.

Rejection of Claims Pursuant to 35 U.S.C. § 103(a)

Claims 37, 38, 55, and 57-68 were rejected pursuant to 35 U.S.C. § 103(a) over either Carter or Cerami in view of Ala-Kokko, Mardon, Beresford, and Flier. In the Examiner's view, mesenchymal cells which are removed from the body are "immunologically isolated," as that phrase was used in the (now canceled) claims. The newly added claims do not recite "immunologically isolated" stromal cells. Instead, the pending claims recite that the stromal cells are contained in a porous,

implantable container that physically isolates the cells from immune cells of an animal into which the container is implanted. Neither Carter nor Cerami discloses transfected stromal cells in such a container. The Applicants respectfully contend that no permissible combination of the references cited by the Examiner teaches or suggests the containers recited in the pending claims, and that this rejection is inapplicable to those claims.

The Examiner observes that Mardon teaches use of an implanted diffusion chamber containing marrow cells. The Applicants note, however, that the marrow cells disclosed in Mardon were not isolated marrow stromal cells (i.e., they were just a mixture of marrow cells), and did not comprise an expressible gene construct (i.e., as recited in the pending claims). Neither Mardon nor any other reference cited by the Examiner discloses that transfected, isolated marrow stromal cells can be maintained in a container of the type recited in the pending claims. In view of the relatively undeveloped state of the art of stromal cell isolation, culture, and transfection at the time the present invention was made, the Applicants respectfully contend that no combination of Mardon and other references cited by the Examiner can fairly be considered to teach every element that is recited in the pending claims. The Examiner is respectfully requested not to reject any of the pending claims pursuant to 35 U.S.C. § 103(a) over a combination of the references cited by the Examiner.

Summary

The Applicants respectfully submit that each of claims 69-112, is in condition for allowance. Allowance of each of these claims is respectfully requested at the earliest possible date.

Respectfully submitted,

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(Date)

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